REMARKS

Claims 1 and 8-10 stand rejected under 35 USC 112, first paragraph, as non-enabling. Specifically, the Examiner contends that the phrase "component of MAPG or a chemical equivalent of MAPG" in claim 1 is non-enabling because only a single undisclosed species of *mycobacterium* is disclosed.

The Examiner's contention the species of *Mycobacterium* from which the MAPG was obtained was not disclosed is incorrect. Review of the specification, for instance, Examples 10 and 11, clearly state that the *Mycobacterium* sub-fractions were from heat killed *Mycobacterium bovis* (BCG). This *Mycobacterium* was used to determine which sub-fraction prevented IDDM without causing the lupus like syndrome. Further, page 17, lines 10 and 11, states that mice receiving this MAPG sub-fraction did not develop IDDM or hemolytic anemia.

Further, enclosed is data (see Appendix A) showing that MAPG from two representative strains of *Mycobacterium*, namely *Mycobacterium tuberculosis* and *Mycobacterium bovis*, prevented the development of type 1 diabetes in NOD/Lt mice (see attached Fig. 1). Additional data demonstrating that a sub-component of MAPG, namely arabinogalactan peptidoglycan (APG) provides protection against Type 1 diabetes is also provided (see attached Fig. 2). Applicants will provide the Examiner a declaration including this data once it is completed.

The specification and the enclosed data show that MAPG, and components of MAPG, from representative species of *Mycobacterium* is effective against IDDM. Consequently, the specification is enabling for the scope of the claimed invention.

Claim 1 stands rejected under 35 USC 102(a) as being anticipated by Stosic-Grujicic. Claims 1 and 10 also stand rejected under 35 USC 103(a) as being anticipated by Stosic-Grujicic. These rejections are respectfully traversed.

Stosic-Grujicic teaches a method of treating autoimmune diabetes in mice by administering 10 to 50 micrograms per injection of well-defined immunomodulatory *Mycobacterium* components derives from the cell wall, a trehalose-dimycolate (TDM) and Purified Protein Derivative (PPD). In comparison, applicants claim a method of immunomodulatory therapy using MAPG. The Examiner contends that TDM and PPD are equivalent to MAPG. As discussed below, the Examiner's contention is incorrect.

MAPG is considered to be the cell wall skeleton of mycobacterium. It has been well characterized by Professor Brennan's group at Colorado State University (see attached copies of

Brennen and Nikaido *Ann. Rev. Biochem. 64:29-63,* 1995 and Brennen *Tuberculosis* 83(1-3):91-97, 2003). It is an insoluble complex consisting of peptidoglycan, which is linked to polysaccharide side chains. The polysaccharide chains have mycolic acids esterified to the distal ends of the polysaccharide side chains. Thus, MAPG is a complex consisting of lipids, sugars and peptides. To obtain MAPG, the bacteria are disrupted and the skeleton extracted using detergent SDS.

In contrast, PPD consists of a number of soluble proteins that are secreted by the bacterial. Unlike MAPG, PPD is not part of the bacteria's cell wall. TDM are extractable glycolipids, also called cord factor and are a member of the mycolic acid family. TDM, however, are different from the mycolic acids that are esterified to the arabinogalactan (polysaccharide side chains) of MAPG. TDM and other lipids are intercalated into the lipid environment provided by the mycolic acids of MAPG. These lipids, such as TMD, PIM and SL are removed from MAPG during the extraction process. Thus PPD and TDM are different compounds to MAPG. Since Stosic-Grujicic fails disclose immunomodulatory therapy using MAPG as claimed, claims 1 and 10 are not anticipated or obvious in view of Stosic-Grujicic.

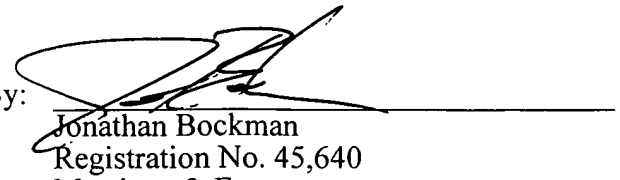
The Examiner has rejected claims 1 and 8-10 under 35 USC 112, second paragraph, as being indefinite. Specifically, the Examiner finds the use of the abbreviation IDDM in claim 1 unclear. The Examiner also finds the phrases "a component of MAPG" or "a chemical equivalent of MAPG" in claims 1 and 9 unclear. Claims 1 and 9 have been amended in accordance with the Examiner's suggestions to overcome these rejections. Since these amendments only require cursory review, these amendments should be entered after the final office action.

For the foregoing reasons, a notice of allowance is solicited.

In the event that the transmittal letter is separated from this document and the Patent and Trademark Office determines that an extension and/or other relief is required, applicant petitions for any required relief including extensions of time and authorizes the Commissioner to charge the cost of such petitions and/or other fees due in connection with the filing of this document to **Deposit Account No. 03-1952** referencing docket no. 229752000600.

Respectfully submitted,

Dated: March 16, 2004

By: 

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